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EXAMINER

SRIVASTAVA, KAILASH C

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 09/10/2002

9

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/807,541

Applicant(s)

AKIMOTO ET AL.

Examiner

DR. Kailash C. Srivastava

Art Unit

1651

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 06/21/2002 (Paper Number 8).
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-43 and 45-80 is/are pending in the application.
- 4a) Of the above claim(s) 15-29, 45-51, 59-64 and 74-90 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-14, 30-43, 52-58 and 65-73 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4 and 6. 6) ☐ Other: \_\_\_\_\_

## **DETAILED ACTION**

1. Applicants' Preliminary amendment filed April 13, 2001 (Paper Number 3) is acknowledged and entered.
2. Claim 44 has been cancelled.
3. Claims 3, 7-10, 12-13, 17-26, 30-33, 36-43, 45, 49-51 have been amended.
4. Claims 52-80 have been added.
5. Applicants' response filed June 21, 2002 (Paper Number 8) to election requirement in Office Action of May 21, 2002 (paper number 7) is acknowledged and entered.
6. Claims 1-43 and 45-80 are pending

### ***Restriction/Election***

7. Applicant's election with traverse of Group I, Claims 1-14, 30-43, 52-59 and 65-73 in response filed June 21, 2002 (Paper Number 8) is acknowledged and entered.

The traversal is on the ground (s) that the instant application was filed under §371 and as such applicants are entitled to "a unity of invention standard" and a search of all the groups would not place an additional burden on the examiner. This is not found persuasive because of the reasons of record on page 2, item 3 in Office Action of May 21, 2002 (paper number 7). Moreover, the search for each of the distinct inventions of Groups I-V is not co-extensive particularly with regard to the literature search. Further, a reference that would anticipate the invention of one group would not necessarily anticipate or even make obvious another group. Finally, the condition for patentability is different in each case. Thus, it will be an undue burden to examine all of the inventive Groups in one application. The restriction requirement is, therefore, still deemed proper and is made FINAL.

Accordingly, Claims 15-29, 45-51, 60-64 and 74-80 are withdrawn from further consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Upon further review, it was noted that Claim 59 depends from a non-elected claim (Claim 15) and should have been included in Group II (Not Group I). Accordingly, Claim 59 is also withdrawn from consideration as being drawn to a non-elected invention.

8. Claims 1-14, 30-43, 52-58 and 65-73 are examined on merits.

### **ABSTRACT**

9. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). The abstract of the disclosure is objected to because the abstract is in two separate paragraphs. See MPEP § 608.01(b). Appropriate correction is required.

### **Claim Rejections - 35 U.S.C. § 101**

10. The following is a quotation of 35 U.S.C. § 101 that form the basis for the rejections under this section made in this Office action:

***Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.***

11. Claims 1-3, 7-14, 34-36 and 52-58 are rejected under 35 U.S.C. § 101 as being drawn to nonstatutory subject matter. As written, the claims are drawn to a biological material *per se*, which is a product of nature. Consequently, the claim does not embody patentable subject matter as defined in 35 U.S.C. § 101. See, e.g., American Wood v. Fiber Disintegrating Co., 90 U.S. 566 (1974); American Fruit Growers v. Brogdex Co., 283 U.S. 1 (1931); Funk Brothers Seed. Co. v. Kalo Inoculant Co. 33 U.S. 127 (1948); Diamond v. Chakrabarty, 206 U.S.P.Q. 193 (1980). The Examiner suggests that applicant use the language "an isolated, biologically pure microorganism" in connection with the microorganism to identify a product that is not found in nature.

### **Claim Rejections - 35 U.S.C. § 112**

12. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

***The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.***

13. Claims 1-14, 30-43, 52-58 and 65-73 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims are directed to a composition obtained by culturing a microorganism, the said microorganism is *Mortierella alpina*. The

microorganism *Mortierella alpina* is essential to the invention recited in those claims. It must therefore be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. If the microorganism is not so obtainable or available, a deposit of the microorganism in a recognized depository may satisfy the requirements of 35 U.S.C. §112.

In order to certify that the deposit meets the criteria set forth in 37 C.F.R. §§ 1.801-1.809, applicants may provide assurance of compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and

(d) the deposit will be replaced if it should ever become inviable.

Applicant is directed to 37 CFR § 1.807 which states:

(b) A viability statement for each deposit of a biological material defined in paragraph (a) of this section not made under the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure must be filed in the application and must contain:

(1) The name and address of the depository;

(2) The name and address of the depositor;

(3) The date of deposit;

(4) The identity of the deposit and the accession number given by the depository;

(5) The date of the viability test;

(6) The procedures used to obtain a sample if the test is not done by the depository; and

(7) A statement that the deposit is capable of reproduction.

Applicant is also directed to 37 CFR § 1.809(d) which states:

(d) For each deposit made pursuant to these regulations, the specification shall contain:

- (1) The accession number for the deposit;
- (2) The date of the deposit.

14. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

***The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.***

15. Claims 7-9, 31-39, 42-43, 55-57, 59 and 66-73 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- The phrase "culture liquid cloudy" in claims 7, 9, 37, 39, 55 and 57 renders those claims indefinite because it is not clear what is meant by the word, "Cloudy". The metes and bounds for the said phrase are not defined. Applicants should clarify the phrase "culture liquid cloudy".
- The phrase "artificially treating" or "artificial treatment" in claims 8-9, 38-39, 53, 56-57 and 70 render those claims indefinite because the metes and bounds for the said phrase are not defined. Applicants should define the phrase "artificially treating" or "artificial treatment".
- The word, "directly" renders claim 35 indefinite because this word in and by itself does not establish metes and bounds. Applicants should define the word "directly" in context of the claimed invention.
- Claim 58 recites the limitation "arachidonic acid" at line 2 after the word "are". There is insufficient antecedent basis for this limitation in the cited claim, because Claim 12 from which Claim 58 depends does not cite "arachidonic acid".

All other cited claims depend directly or indirectly from the rejected claims and are, therefore, also rejected under 35 U.S.C. § 112, second paragraph for the reasons set forth above.

### ***Claim Rejections – 35 U.S.C. § 102***

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

***A person shall be entitled to a patent unless –***

**(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.**

17. Claims 1-3, 7-9, 12, 30, 32-33, 53, 56 and 68 are rejected under 35 U.S.C. §102(b) as anticipated by Fukui (Bioindustry, 12, 36-46, 1995), with evidence provided by Stedman's Medical Dictionary (Williams and Wilkins, Baltimore, 1995, Page 1851, Column 2, Lines 41-47).

Claims recite a filamentous fungal microorganism, which when grown on a solid culture medium extracellularly secretes a lipid surrounded by a lipid vesicle, wherein said lipid contains unsaturated fatty acids. The said microorganism is obtained by an artificial treatment of a microorganism that intracellularly accumulates unsaturated fatty acid containing lipid. The said filamentous microorganism upon cultivation in a liquid medium, secretes the said lipid vesicles in the liquid medium from where lipid vesicles are removed, the lipid contained in the lipid vesicles are isolated and from the said lipid, the constituent unsaturated fatty acids are also isolated.

Fukui discloses a microorganism having the capability of extracellularly secreting unsaturated fatty acid containing lipids. Fukui further discloses selection of "lipid and fatty acid secreting" microorganism, the said microorganism when grown on a solid culture medium produces a halo around its colony (page 1, Line 27 and Line 35 to Page 2, Line 2). The said microorganism is obtained through selection on a solid medium after treating with ultraviolet light or EMS a microorganism having the capability of intracellularly accumulating a lipid (Page 4, Lines 28-34 palmitic acid is a lipid). Thus, the lipid excreting strain was obtained through mutation (Page 4, Line 10-11) of a microorganism capable of accumulating lipids intracellularly. Fukui further discloses that a *Trichosporon* strain (a filamentous fungus, see Stedman's Dictionary 1851, Column 2, Lines 41-47), when grown in a liquid medium extracellularly secretes lipids as triglycerides (i.e. TG) with high efficiency and the component fatty acids include oleic and linoleic acids among others (Page 10, Lines 2-12 and Page 11, Lines 5-7). Please note that Fukui discloses production of a lipid containing halo around the periphery of the microbial colonies and also cultivation of a microorganism that extracellularly secretes lipids in a liquid culture medium and the said lipid is comprised of unsaturated fatty acids, i.e. the prior art method of cultivating a microorganism having the capability of extracellularly secreting lipids when grown on a solid or a liquid medium, inherently must function as claimed (i.e., to extracellularly secrete lipid vesicles) because the microorganism disclosed in the prior art reference has the same capabilities and is

being cultivated in the same way (See e.g., *In re Best*, 195 USPQ 430, 433-CCPA 1977) as is recited in the claimed invention.

Therefore, the reference is deemed to anticipate the cited claims.

Please note that Stedman's Medical dictionary is merely to support that *Trichosporon* is a filamentous fungus and is not cited as a prior art reference.

18. Claims 1-6, 14, 34-37, 52, 55 and 69 are rejected under 35 U.S.C. §102(b) as anticipated by Fragrance Journal (6, Page 67-75, 1996) with evidence provided by Stedman's Medical Dictionary (Williams and Wilkins, Baltimore, 1995, Page 121, Column 1, Lines 44-48).

Claims recite a filamentous fungal microorganism, *Mortierella alpina* which when grown on a solid culture medium extracellularly secretes a lipid surrounded by a lipid vesicle, wherein said lipid contains unsaturated fatty acids that have 18 carbons and  $\geq 3$  double bonds or  $\geq 20$  carbons and  $\geq 2$  double bonds. The said unsaturated fatty acid is anyone of  $\gamma$ -linolenic acid, arachidonic acid, DHA and 9 $\omega$  highly unsaturated fatty acids. The said microorganism secretes a lipid wherein  $\geq 10\%$  of the total lipid is arachidonic acid.

Fragrance Journal discloses cultivation of *Mortierella alpina* on a solid medium to produce arachidonic acid. The amount of arachidonic acid in the total lipid produced on the said solid medium calculates out to be  $>10\%$  ((Table 2, Lines 23-25,43 and 44). Archidonic acid is a C18 unsaturated fatty acid that contains 4 double bonds (see Stedman's Medical Dictionary, Williams and Wilkins, Baltimore, 1995, Page 121, Column 1, Lines 44-48).

Therefore, the reference is deemed to anticipate the cited claims.

Please note that Stedman's Medical dictionary is merely to support the structure of arachidonic acid and is not cited as a prior art reference.

19. Claim 11 is rejected under 35 U.S.C. §102(b) as anticipated by Higashiyama et al (Patent Abstract of Japan 06153970).

Claim recites a filamentous fungus having the capability of extracellularly secreting unsaturated fatty acid containing lipid.



Higashiyama et al disclose that unsaturated fatty acid containing lipid are produced when a microorganism of genus *Mortierella*, subgenus *Mortierella* is aerobically cultured (Abstract, Lines 5-8). Applicants have admitted on record that a microorganism of the genus *Mortierella*, subgenus *Mortierella* is a filamentous fungus.

Therefore, the reference is deemed to anticipate the cited claim.

### **Claim Rejections - 35 U.S.C. § 103**

20. The following is a quotation of 35 U.S.C. §103(a) which forms the basis for all obviousness rejections set forth in this Office action:

**(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.**

21. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

22. Claims 1-14, 30-43, 52-58 and 65-73 are rejected under 35 U.S.C. § 103 (a) as obvious over Fukui (Bioindustry, 12, 36-46, 1995), in view of Fragrance Journal (6, Page 67-75, 1996) with evidence provided by Stedman's Medical Dictionary (1995, Williams and Wilkins, Baltimore, Page 121, Column 1, Lines 44-48 and Page 1851, Column 2, Lines 41-47).

Claims recite a filamentous fungal microorganism, *Mortierella alpina* that is capable of secreting lipids extracellularly. The said microorganism is obtained by artificially treating a microorganism (i.e., mutating a microorganism) that accumulates lipids intracellularly. The resultant said microorganism when cultivated on a solid or in a liquid medium extracellularly secretes lipids (triglyceride and unsaturated fatty acids), the said lipids are in lipid vesicles. The said lipid vesicles are separated from the culture medium and lipid contained therein as well as the triglyceride and unsaturated fatty acids comprising said lipid are isolated. The claims further recite methods to obtain and select such a microorganism through mutation, cultivation of the resultant microorganism in a liquid medium to produce the said lipid

vesicles. Claims further recite separating the said lipid vesicles from the culture medium, isolating the said lipid and said unsaturated fatty acids constituting the said lipid. Claims further recite that the said microorganism also carries out a desaturation reaction of fatty acids (e.g.,  $\delta 9$  desaturation reaction).

As stated in item 17 *supra*, Fukui discloses a microorganism having the capability of extracellularly secreting unsaturated fatty acid containing lipids. Fukui further discloses selection of "lipid and fatty acid secreting" microorganism, the said microorganism when grown on a solid culture medium produces a halo around its colony (page 1, Line 27 and Line 35 to Page 2, Line 2). The said microorganism is obtained through selection on a solid medium after treating a microorganism having the capability of intracellularly accumulating a lipid with ultraviolet light or EMS (Page 4, Lines 28-34, palmitic acid is a lipid). Thus, the lipid excreting strain is obtained through mutation (Page 4, Line 10-11) of a microorganism capable of accumulating lipid intracellularly. Fukui further discloses that a *Trichosporon* strain (a filamentous fungus, see Stedman's Dictionary 1851, Column 2, Lines 41-47) when grown in a liquid medium extracellularly secretes lipids as triglycerides (i.e. TG) with high efficiency and the component fatty acids include oleic and linoleic acids among others (Page 10, Lines 2-12 and Page 11, Lines 5-7). Fukui further discloses fatty acid desaturation during fermentative production of triglyceride by *Trichosporon* (Page 6, Lines 11-13).

Please note that Fukui discloses production of a lipid containing halo around the periphery of the microbial colonies and also cultivation of a microorganism that extracellularly secretes lipids in a liquid culture medium and the said lipid is comprised of unsaturated fatty acids, i.e. the prior art method of cultivating a microorganism having the capability of extracellularly secreting lipids when grown on a solid or a liquid medium, intrinsically must function as claimed (i.e., to extracellularly secrete lipid vesicles) because the microorganism disclosed in the prior art reference has the same capabilities and is being cultivated in the same way (See e.g., *In re Best*, 195 USPQ 430, 433-CCPA 1977) as is recited in the claimed invention. Thus, Fukui discloses a microorganism that extracellularly secretes lipid vesicles when cultivated on a solid or in a liquid medium.

Fukui, however, does not disclose that the filamentous fungal microorganism is *Mortierella alpina* and the extracellularly secreted lipid that the said fungus secretes contains unsaturated fatty acids that have 18 carbons and  $\geq 3$  double bonds or  $\geq 20$  carbons and  $\geq 2$  double bonds. Fukui also does not disclose that the said unsaturated fatty acid is

anyone of  $\gamma$ -linolenic acid, arachidonic acid, DHA and 9 $\omega$  highly unsaturated fatty acids and that the said fungus secretes a lipid wherein  $\geq 10\%$  of the total lipid is arachidonic acid.

As discussed in item 18 *supra*, Fragrance Journal discloses cultivation of *Mortierella alpina* on a solid medium to produce arachidonic acid. The disclosed amount of arachidonic acid in the total lipid produced on the said solid medium calculates out to be  $>10\%$  ((Table 2, Lines 23-25, 43 and 44). Arachidonic acid is a C18 unsaturated fatty acid that contains 4 double bonds (see Stedman's Medical Dictionary, Page 121, Column 1, Lines 44-48).

At the time the invention was made, it would have been obvious to one of ordinary skill in the art to modify Fukui's teachings according to those of Fragrance Journal to include members of genus *Mortierella*, subgenus *Mortierella* in Fukui's screening methods and to analyze for arachidonic acid in the composition of lipid separated from the culture liquid, because both Fukui and Fragrance Journal teach extracellular production of lipid containing vesicles, wherein the lipid in said vesicles is comprised of unsaturated fatty acids. The said vesicles are secreted when a fungus that secretes lipids is cultured on a solid or in a liquid culture medium. Fukui further teaches that the said fungus is obtained by mutating a fungus that has the capability to intracellularly accumulate lipids (page 1, Line 27 and Line 35 to Page 2, Line 2; Page 4, Lines 10-11, 28-34) and the said fungus secretes lipids as triglycerides (i.e. TG) with high efficiency when the said fungus is grown in a liquid medium. The component fatty acids (i.e., oleic and linoleic acids) comprising said lipid are produced through fatty acid desaturation (Page 6, Lines 11-13). The Fragrance Journal beneficially discloses that *Mortierella alpina* when cultivated on a solid medium produces unsaturated fatty acid containing lipid, wherein the said fatty acid is arachidonic acid (i. e., a C18 unsaturated fatty acid that contains 4 double bonds) and the disclosed amount of arachidonic acid in the total lipid produced on the said solid medium calculates out to be  $\geq 10\%$  (Table 2, Lines 23-25, 43 and 44). Accordingly, one having ordinary skill in the art would have been motivated to obtain a filamentous fungus of genus *Mortierella* that extracellularly secretes lipid vesicles containing lipid, wherein lipid is comprised of unsaturated fatty acids and triglycerides and the said unsaturated fatty acid is a C18 unsaturated fatty acid with 4 double bonds (e.g., arachidonic acid) produced through fatty acid desaturation as  $\geq 10\%$  of the total lipid produced in the said medium (said fungus obtained by mutating a fungus that accumulates lipids intracellularly) because Fukui teaches that such a fungus is obtainable through mutation and subsequent screening (page 1, Line 27 and Line 35 to Page 2, Line 2; Page 4, Lines 10-11, 28-34; Page 6, Lines 11-13), while

Fragrance Journal beneficially teaches that *Mortierella alpina* produces an unsaturated fatty comprised of C18 with 4 double bonds (see Stedman's dictionary, Page 121, Column 1, Lines 44-48) the acid being arachidonic acid and wherein said arachidonic acid is  $\geq 10\%$  of the total lipid produced (Table 2, Lines 23-25, 43 and 44).

From the teachings of the cited references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

23. Claims 10 and 40 are rejected under 35 U.S.C. § 103 (a) as being unpatentable over Fukui (Bioindustry, 12, 36-46, 1995), in view of Fragrance Journal (6, Page 67-75, 1996) with evidence provided by Stedman's Medical Dictionary (1995, Williams and Wilkins, Baltimore, Page 121, Column 1, Lines 44-48; Page 1851, Column 2, Lines 41-47) and further in view of Buxton et al (U.S. Patent 4,885,249) and Harman et al (U.S. Patent 5,260,213).

Also claimed is the conversion of microorganism discussed *supra* into protoplasts or spheroplasts.

The teachings of Fukui and Fragrance Journal with the evidence provided by Stedman's Medical Dictionary are relied upon for the reasons set forth above. None of these references expressly teach the conversion of said filamentous fungus into protoplast or spheroplasts.

Buxton et al., beneficially disclose spheroplasts of *Aspergillus niger* (Abstract, Line 12) to conduct transformations. Buxton et al., however do not teach formation of protoplasts from filamentous fungi. Harman et al disclose a method to obtain a number of viable protoplasts of *Trichoderma* sp (Column 6, Lines 54-55 and Column 8, Lines 26-407).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to further modify the microorganisms and methods of Fukui and Fragrance Journal according to the beneficial teachings of Buxton et al., and Harman et al as discussed above. Thus, Buxton et al., and Harman et al., resolve the deficiency of obtaining protoplasts and spheroplasts of the fungal microorganism in the teachings of Fukui and Fragrance Journal discussed in item 22 *supra*. Accordingly, since each one of the cited prior art references teach transformation of a filamentous fungal microorganism to

obtain a microorganism capable of extracellularly secreting unsaturated fatty acid containing lipids in a lipid vesicle, an artisan of ordinary skill would be motivated to combine the teachings from each one of the cited references to obtain a filamentous fungal microorganism or spheroplast or protoplast of such a microorganism that extracellularly secretes unsaturated fatty acid containing lipids contained in a lipid vesicle, wherein the said fatty acid is a C18 unsaturated fatty acid with 4 double bonds (e.g., arachidonic acid) produced through fatty acid desaturation as  $\geq 10\%$  of the total lipid produced in the said medium. None of the cited references teach that when the cited filamentous fungi are cultivated in the liquid media, the culture medium turns "cloudy" or continuous cultivation of the microorganism and harvesting the lipid vesicles or detailed method to convert *Mortierella* sp into spheroplast or protoplast. However, the adjustment of particular conventional working conditions (e.g., culture conditions for cultivating a microorganism, i.e., temperature, pressure, pH, dissolved oxygen or gas, concentration of different nutrients and substrates or additives, duration for culturing and harvesting times or specific cellular types (e.g., sphero- or protoplasts) of a given microorganism and how those cell types are made), is deemed merely a matter of judicious selection and routine optimization which is well within the purview of the skilled artisan and therefore obvious under 35 U.S.C. § 103(a).

From the teachings of the references cited *supra*, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.


### **Conclusion**

24. No Claims are allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (703) 605-1196. The examiner can normally be reached on Monday-Thursday from 7:30 A.M. to 6:00 P. M. (Eastern Standard Time or Eastern Daylight Saving Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn, can be reached on (703) 308-4743 Monday through Thursday. The fax phone number for the organization where this application or proceeding is assigned is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

  
Kallash C. Srivastava, Ph.D.  
Patent Examiner  
Art Unit 1651  
(703) 605-1196

September 9, 2002



CHRISTOPHER R. TATE  
PRIMARY EXAMINER